

Synthesis of H-TAP-Boc molecule

Synthesis of Cbz-TAP

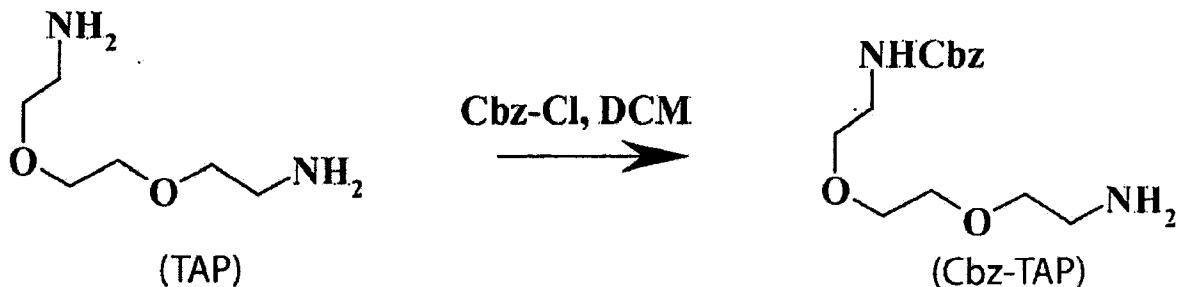


FIG. 1A

Synthesis of Cbz-TAP-Boc

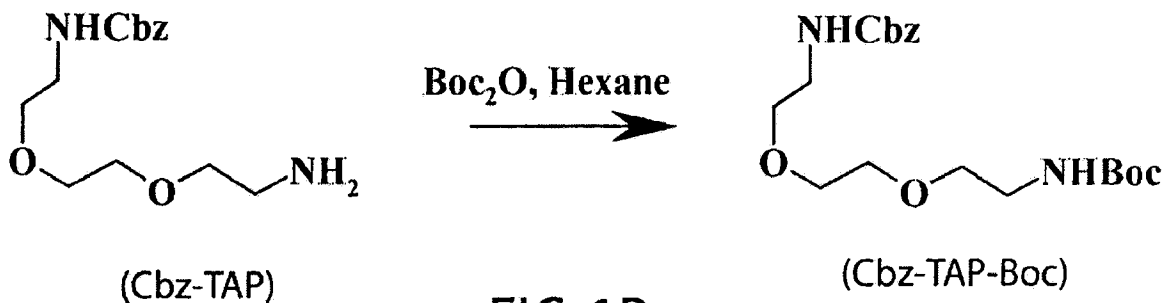


FIG. 1B

Synthesis of Boc-TAP

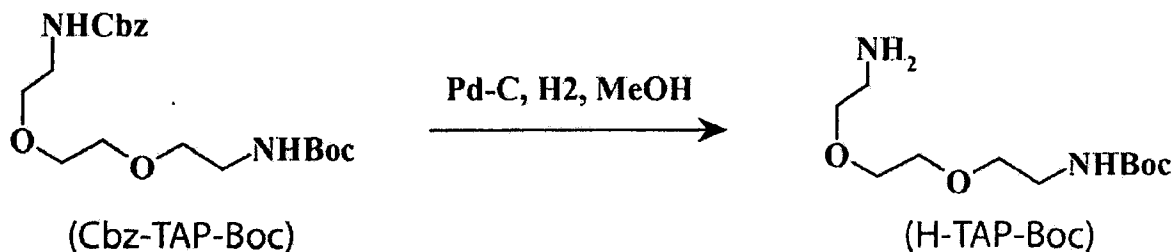


FIG. 1C

Attaching Spacer to Peptide with C-Terminus

Peptide with free C-terminus:

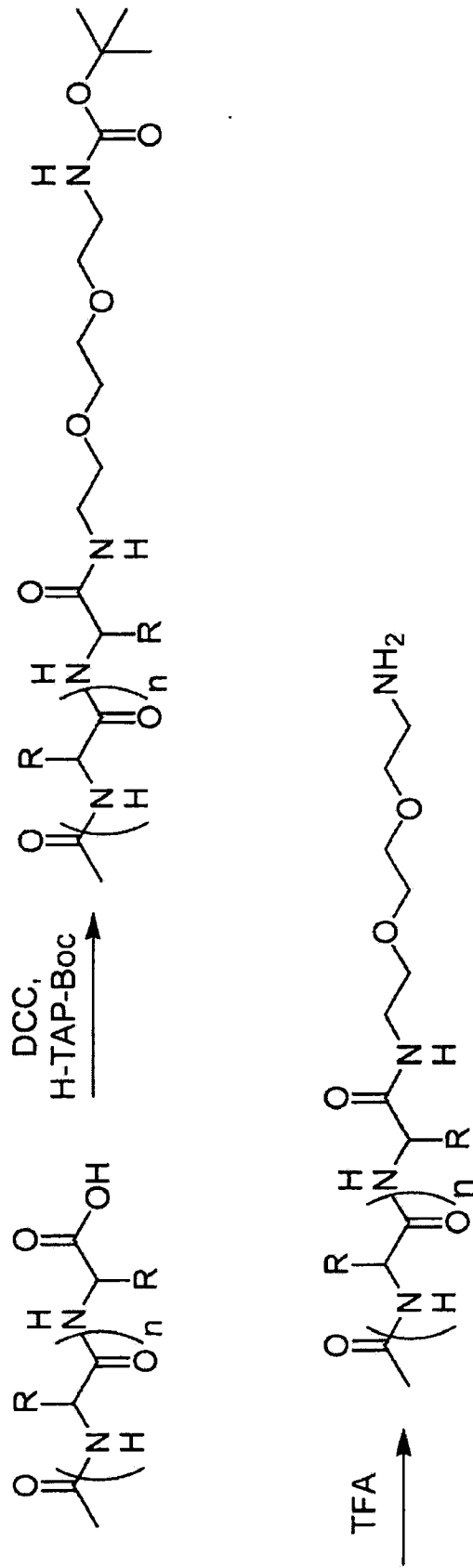


FIG. 2

Attaching Spacer to Peptide with Free Side-Chain Acid

Peptide with free side-chain acid:

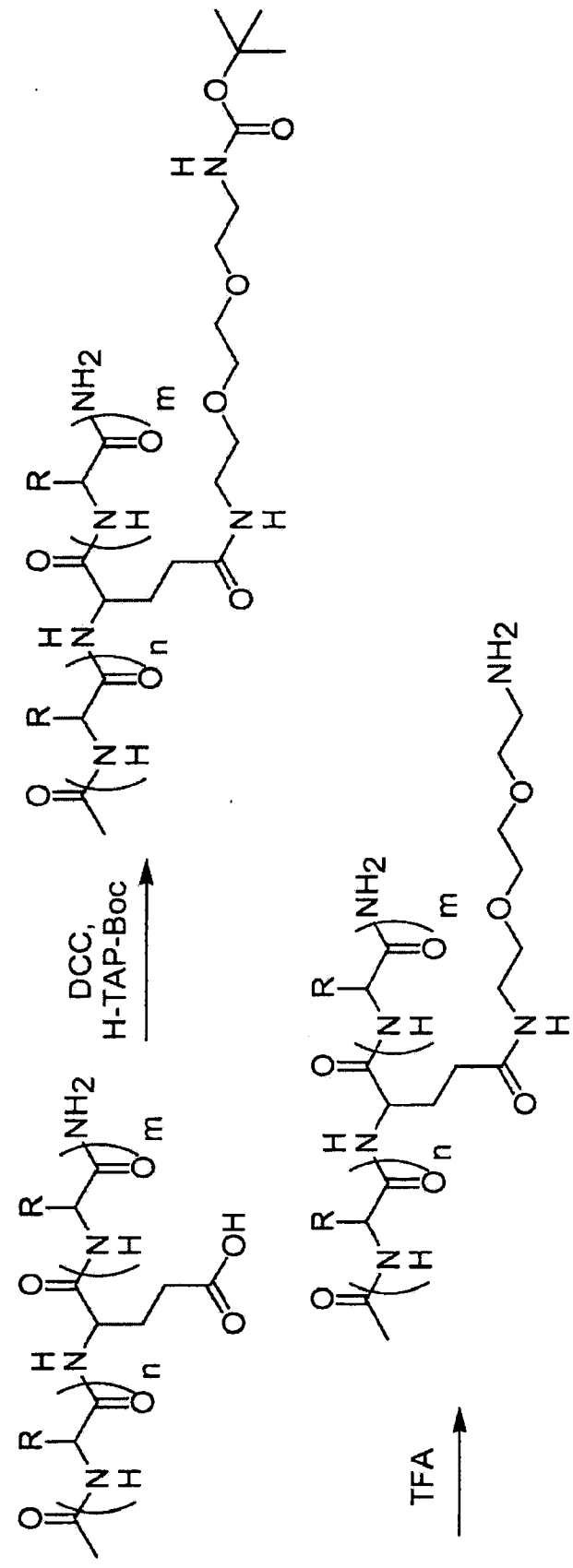


FIG. 3

PEGylation of Peptide, with mPEG-NPC

Peptide with TAP on C-terminus:

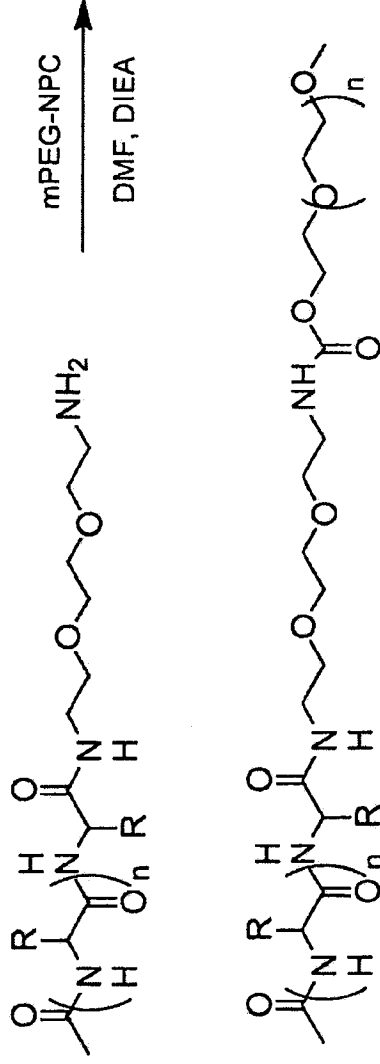


FIG. 4A

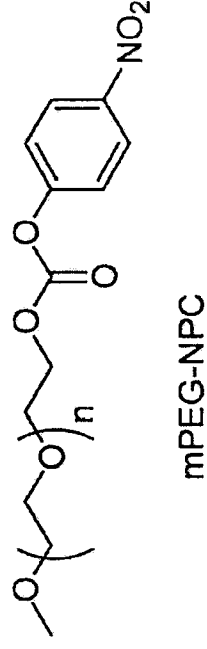


FIG. 4B

PEGylation of Peptide, with mPEG-SPA

Peptide with TAP on C-terminus:

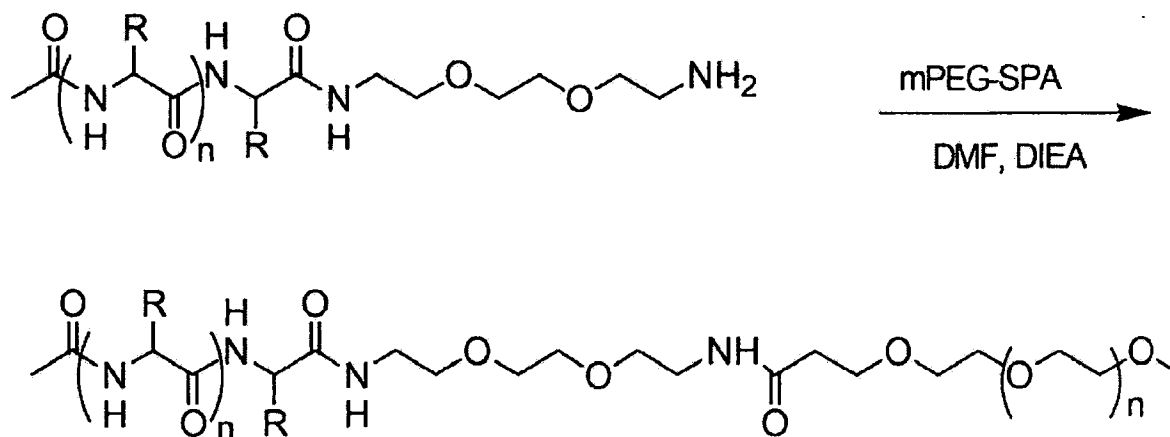
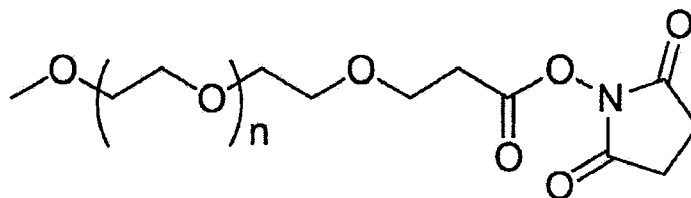


FIG. 5A



mPEG-SPA

FIG. 5B

Attaching Spacer and Synthesizing Peptide

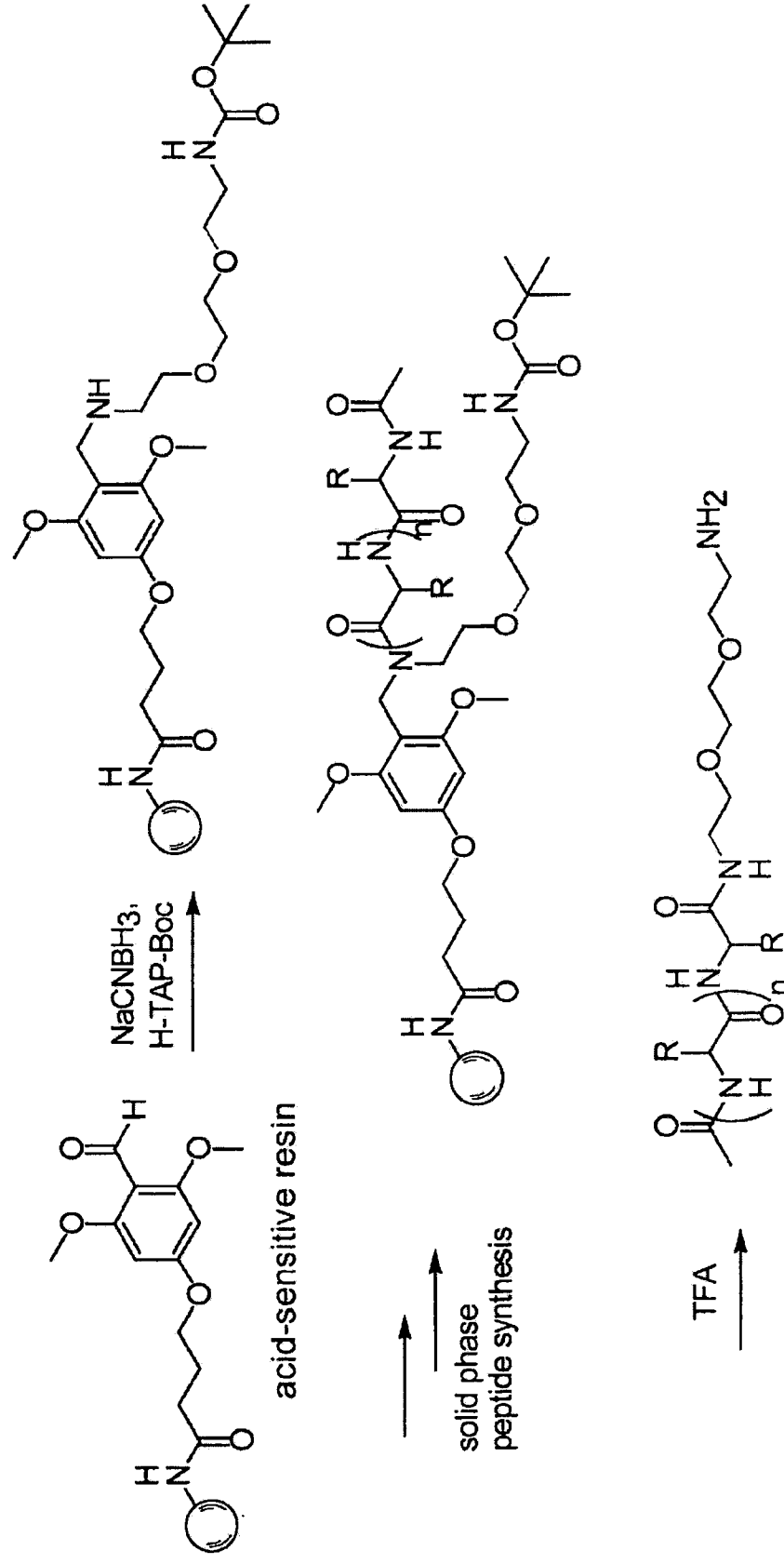


FIG. 6

Synthesis of Peptide Dimer with Spacer, Attached to Resin Synthesis of TentaGel-Linker:

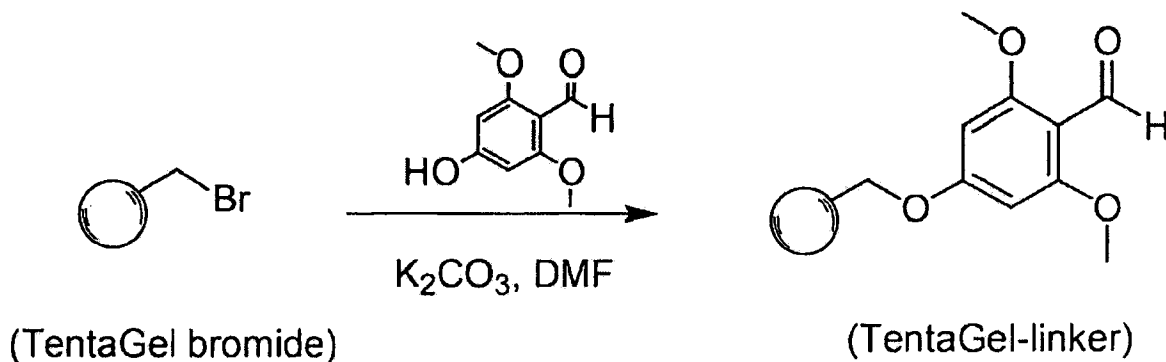


FIG. 7A

Synthesis of TentaGel-Linker-TAP(Boc)

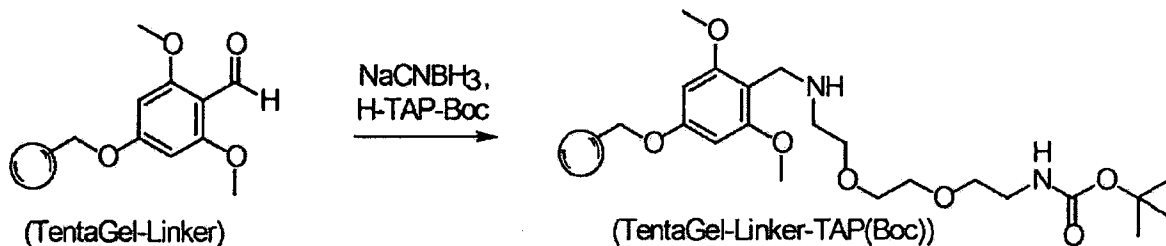


FIG. 7B

Synthesis of TentaGel-Linker-TAP-Lys

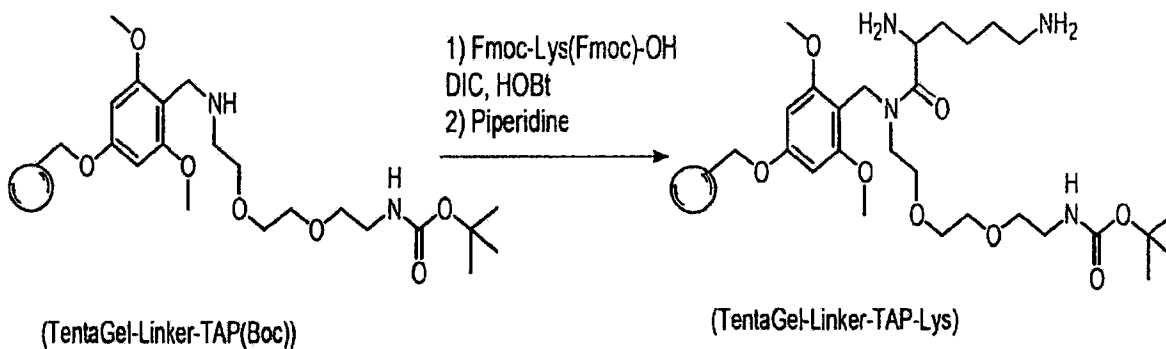


FIG. 7C

Synthesis of TentaGel-Linker-TAP-Lys(Peptide) 2

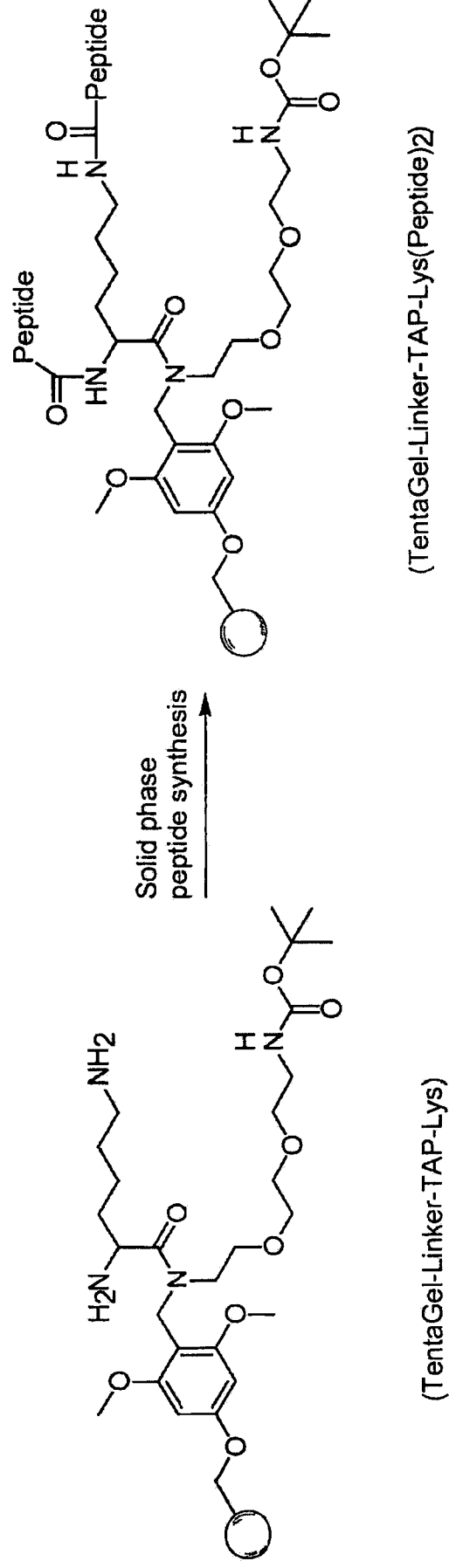


FIG. 7D

Cleavage from Resin

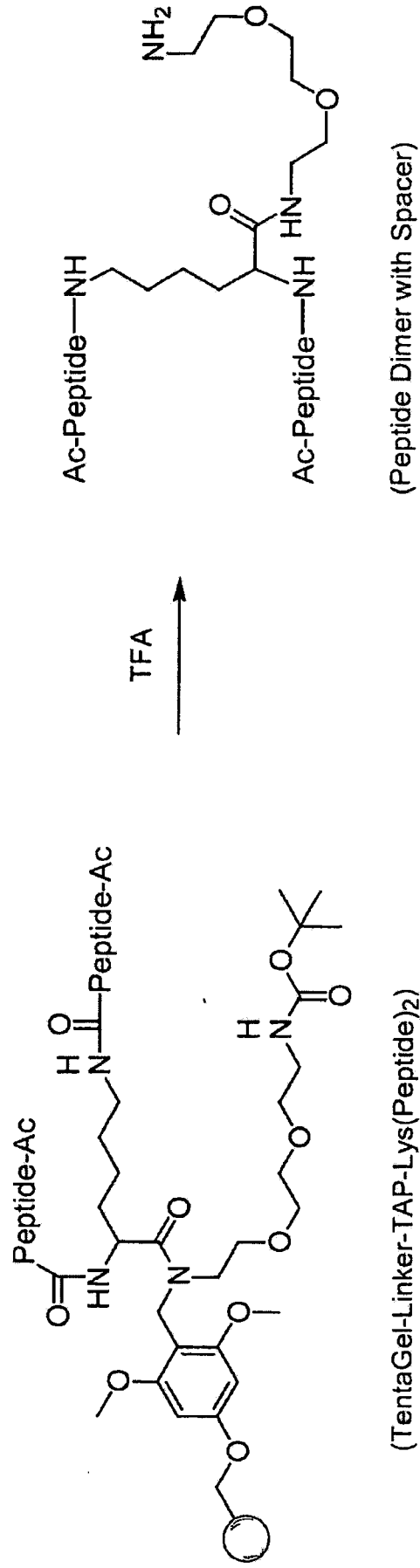
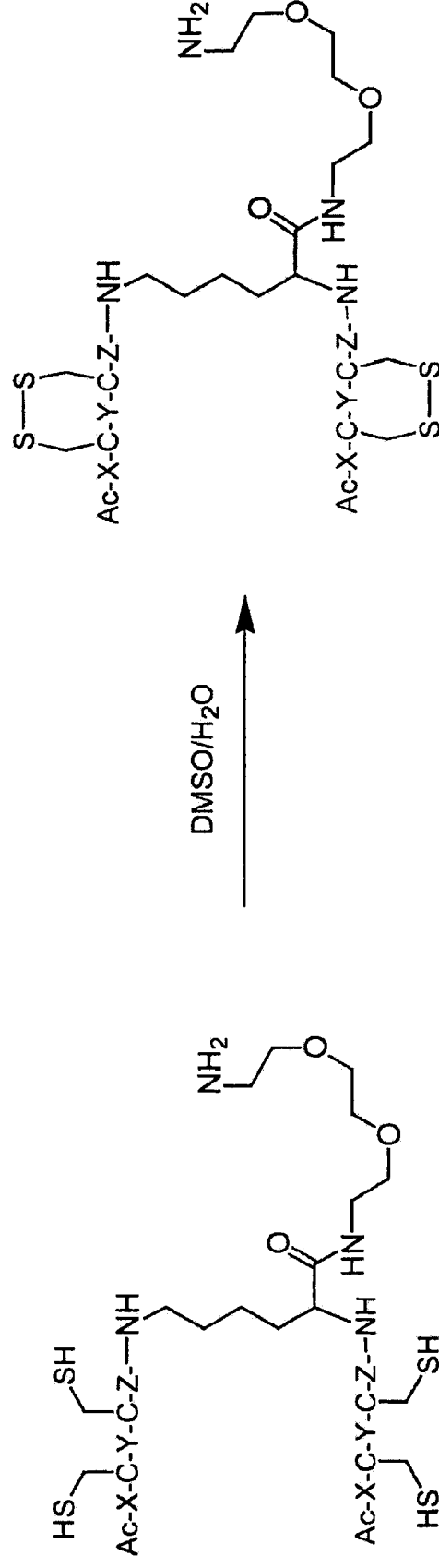


FIG. 7E

Oxidation



Dimeric peptide (XYZ) containing reduced cysteine residues

Dimeric peptide (XYZ) containing oxidized disulfide bonds

FIG. 7F

PEGylation of Peptide Dimer with Spacer, with mPEG-NPC

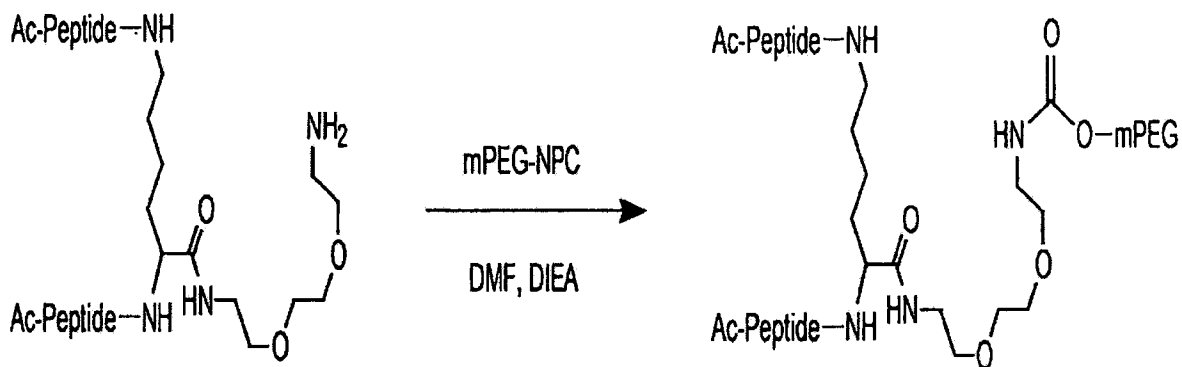


FIG. 8A

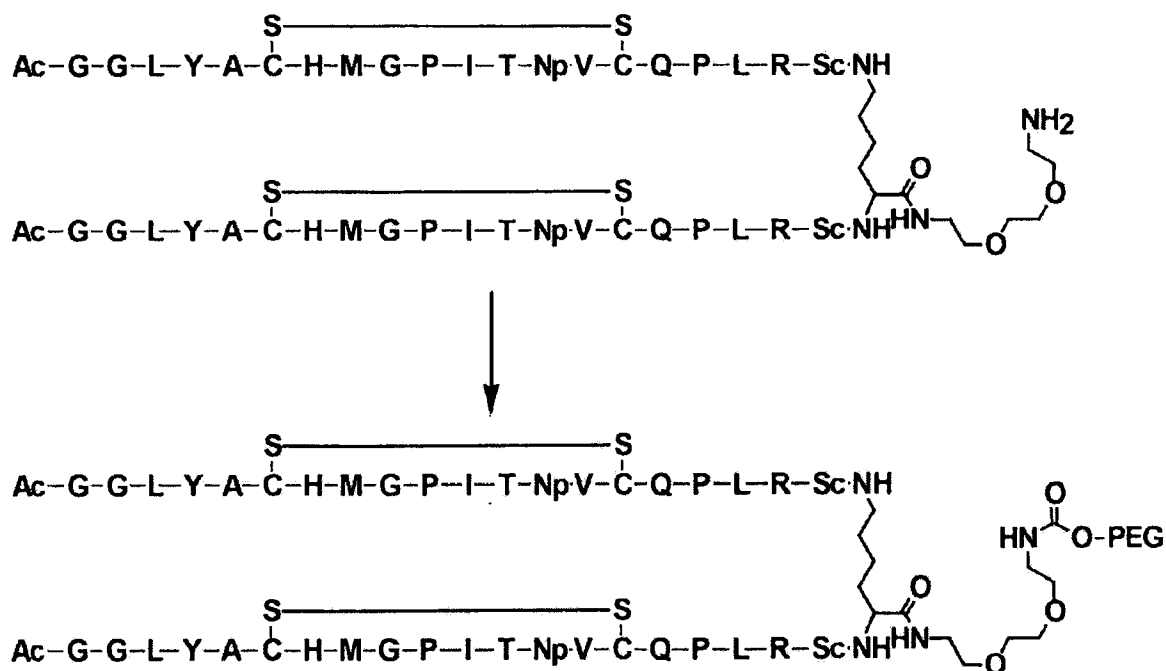


FIG. 8B

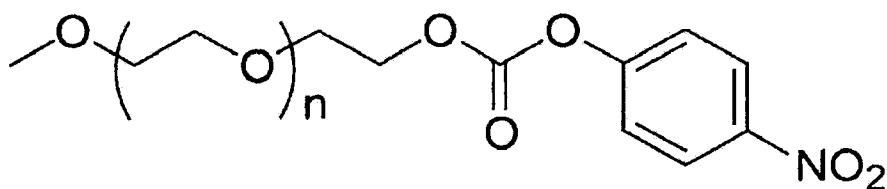


FIG. 8C

PEGylation of Peptide Dimer with Spacer, with mPEG-SPA

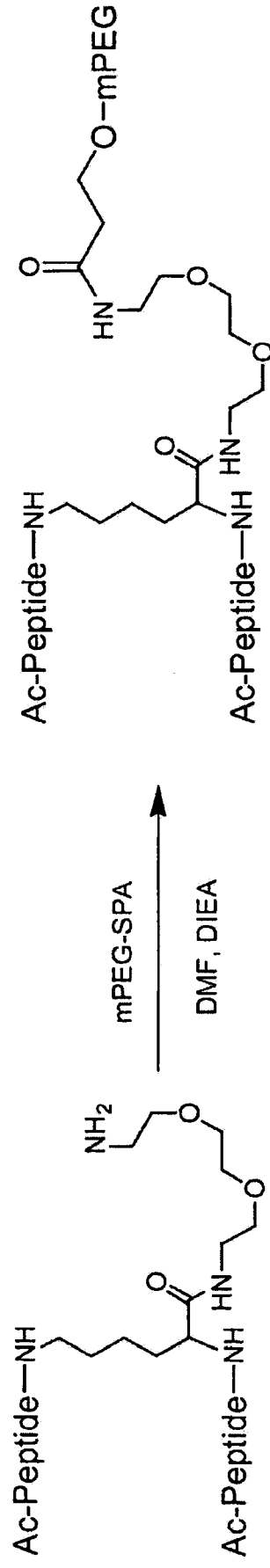


FIG. 9A

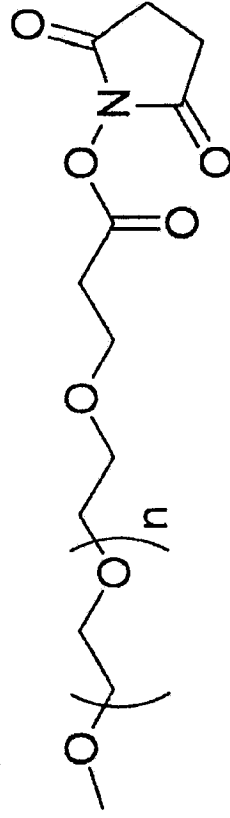


FIG. 9B

Ion Exchange Purification

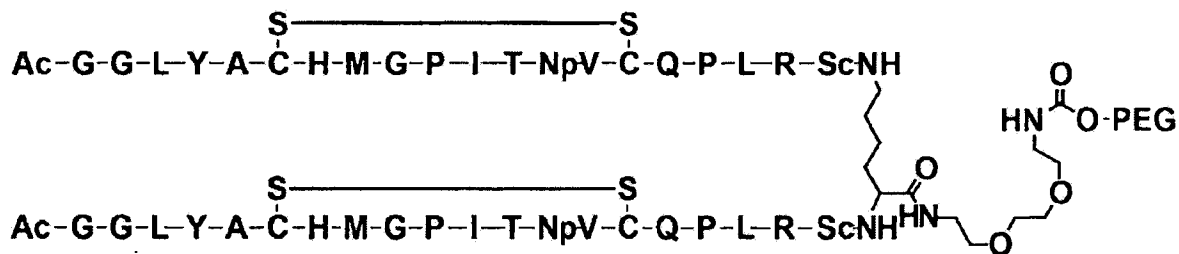
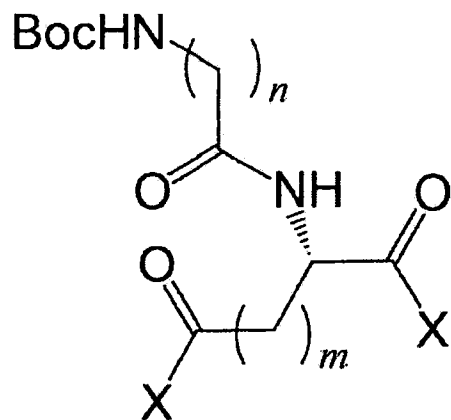


FIG. 10



$m=1-5$, $n = 1-14$, m and n are integers

FIG. 11A

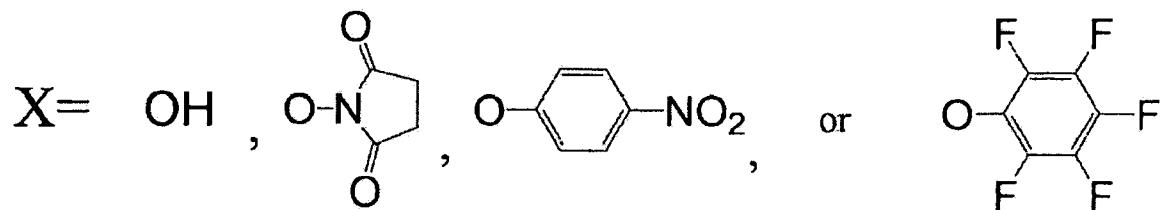
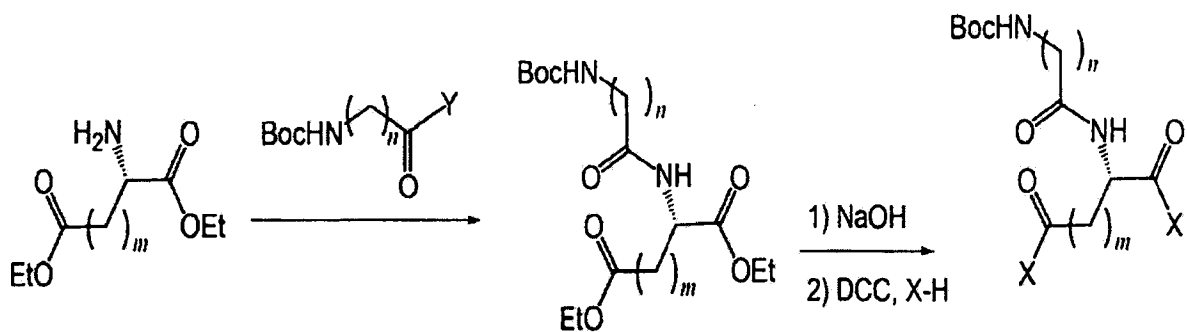
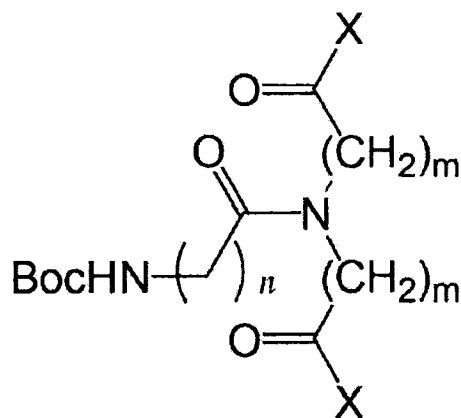


FIG. 11B



$m=1-5$, $n = 1-14$, m and n are integers

FIG. 11C



$m=1-5$, $n = 1-14$, m and n are integers

FIG. 12A

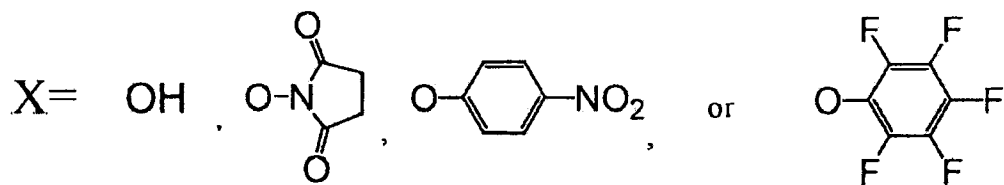


FIG. 12B

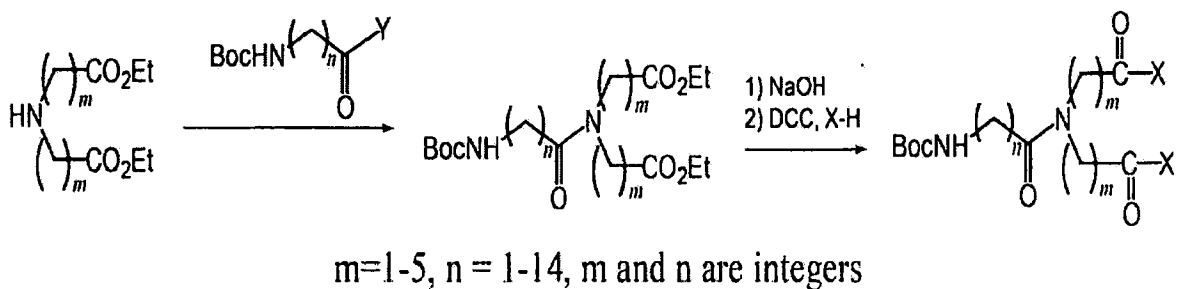
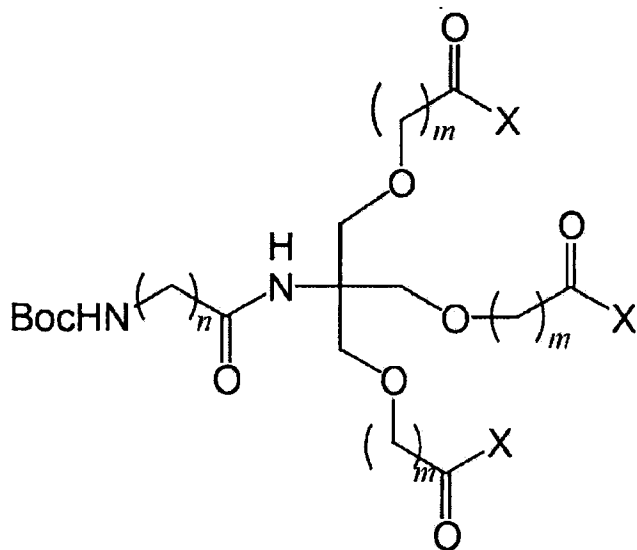


FIG. 12C

Synthesis of Homotrifunctional Molecules
Branched homotrifunctional molecules having the structure



$m=1-2, n = 1-6, m \text{ and } n \text{ are integers}$

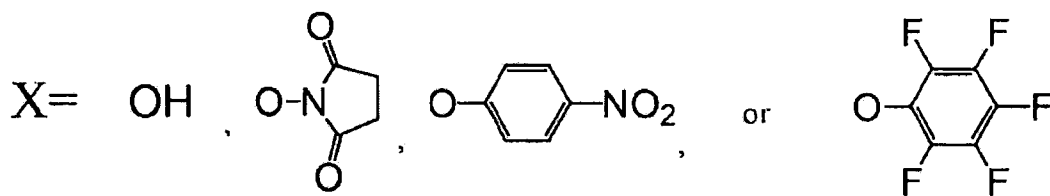
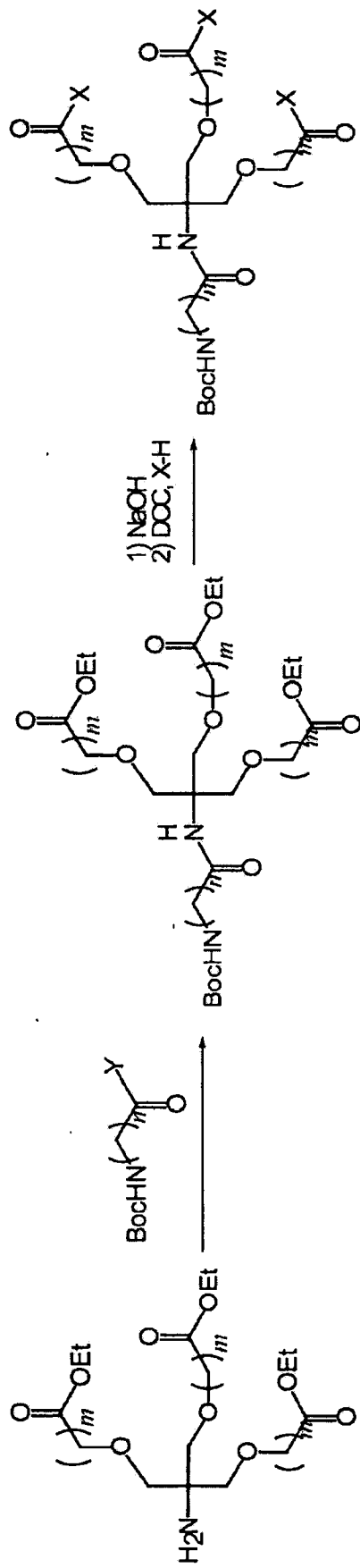


FIG. 13A



$m=1-2, n=1-6, m$ and n are integers

FIG. 13B

C-Terminus Dimerization and PEGylation Using A Trifunctional Molecule

A trifunctional molecule having the structure

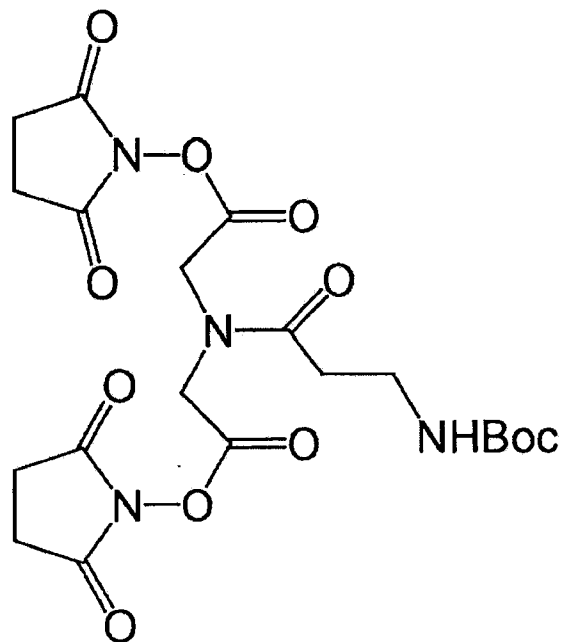


FIG. 14A

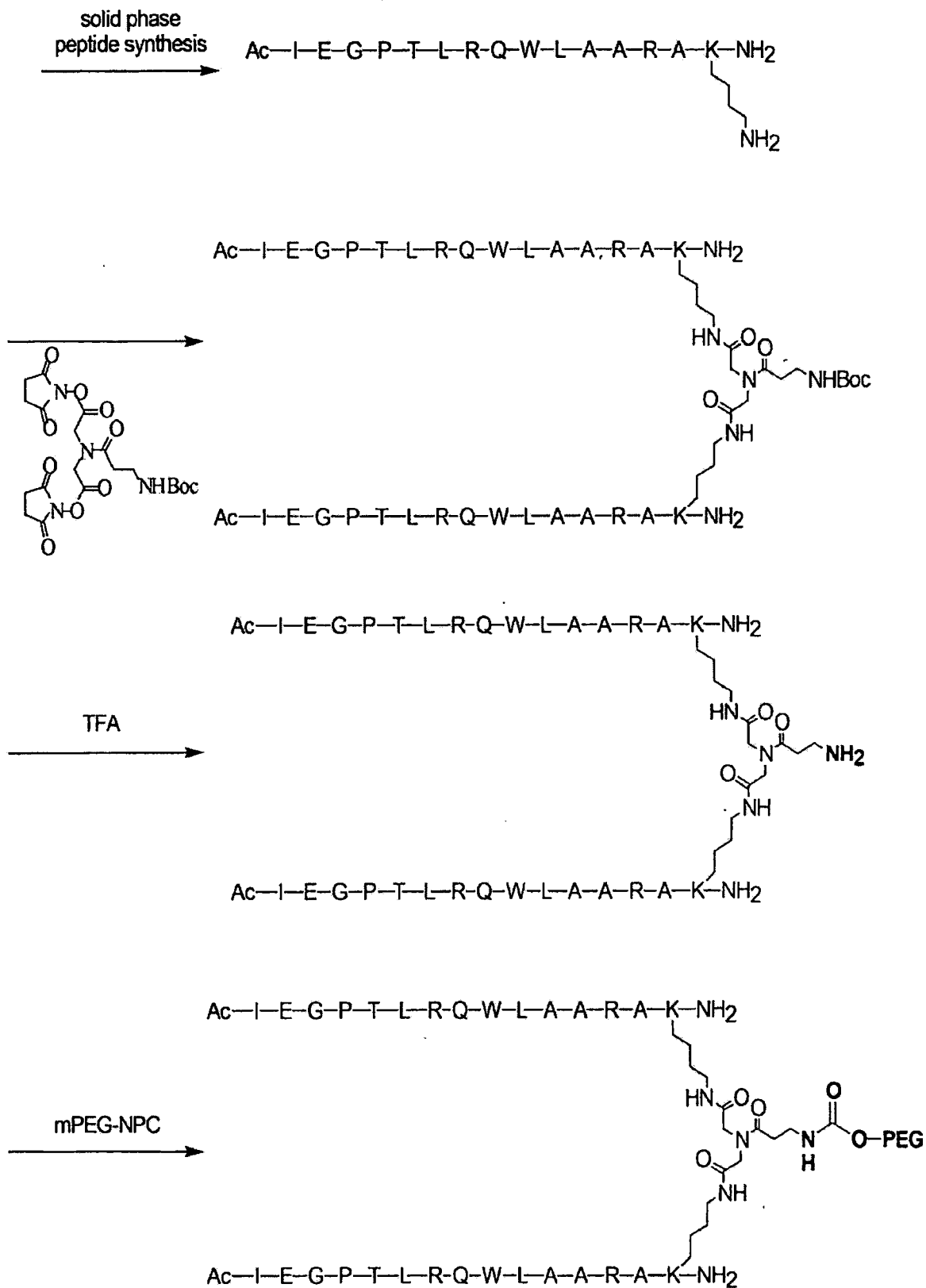


FIG. 14B

N-Terminus Dimerization and PEGylation Using A Trifunctional Molecule

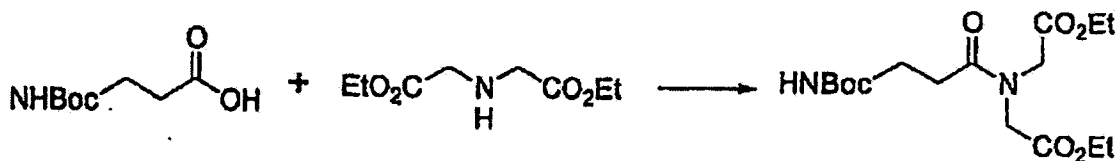


FIG. 15A

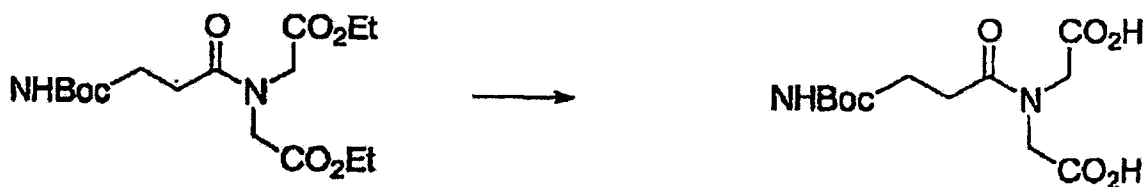


FIG. 15B

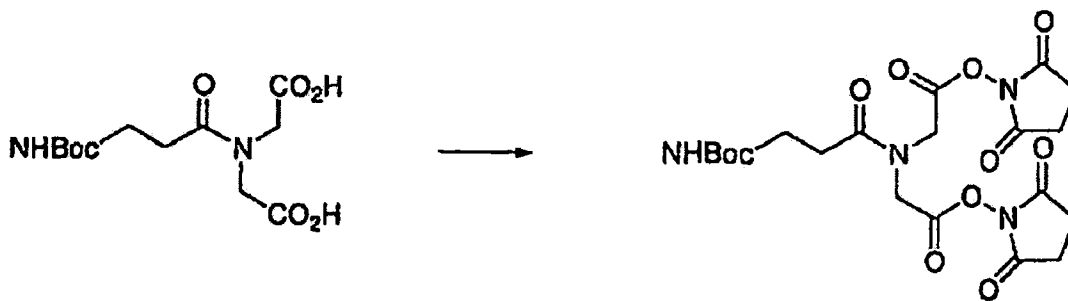


FIG. 15C

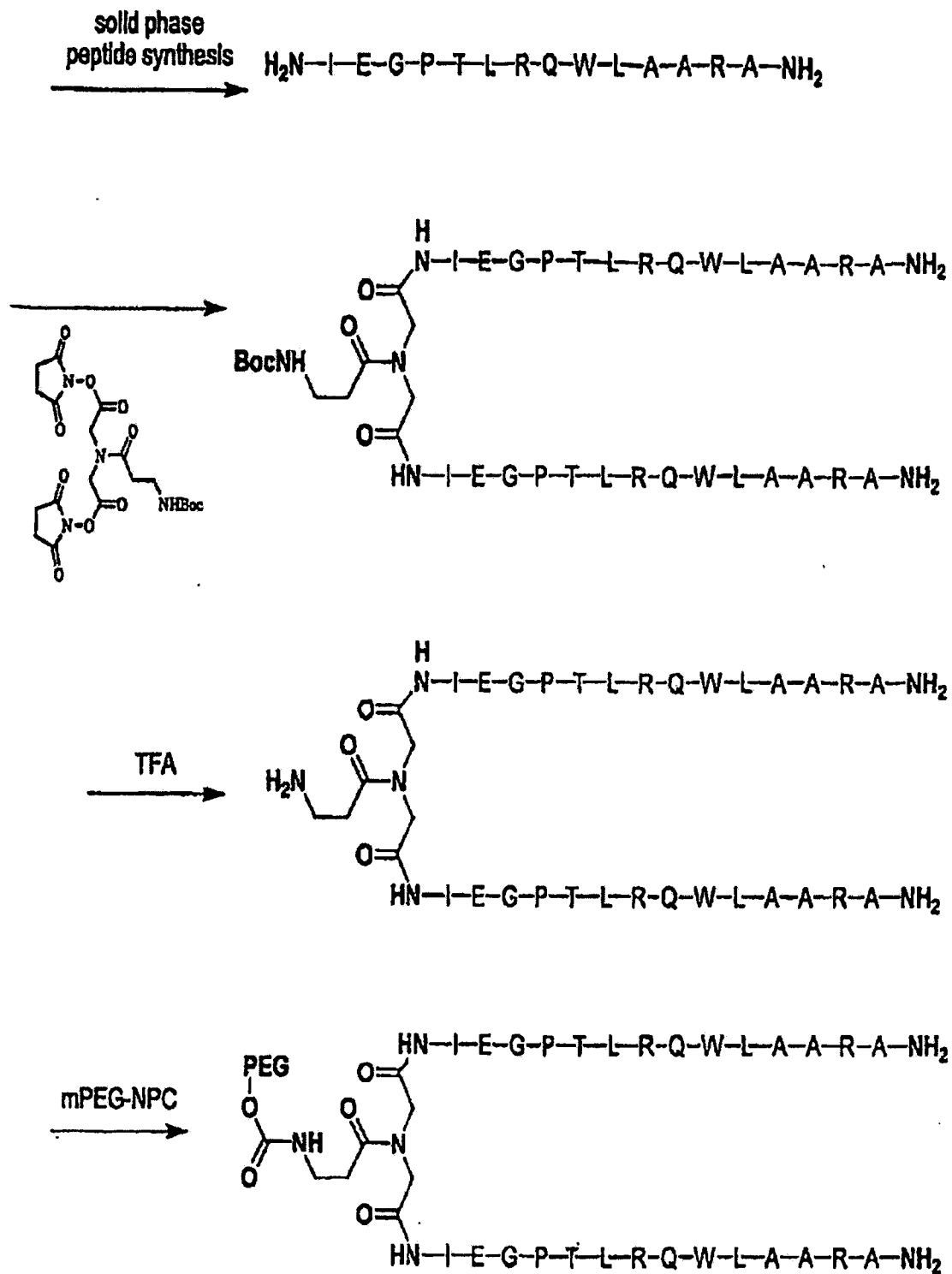


FIG. 15D

A trifunctional molecule having the structure

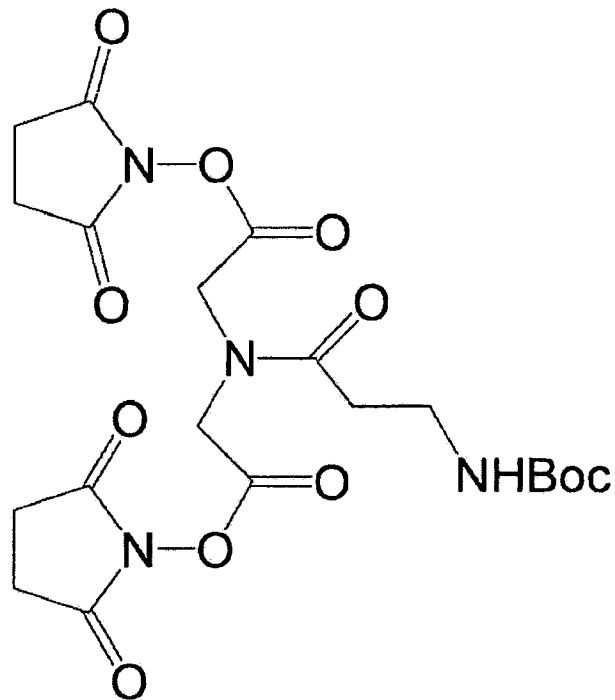


FIG. 16A

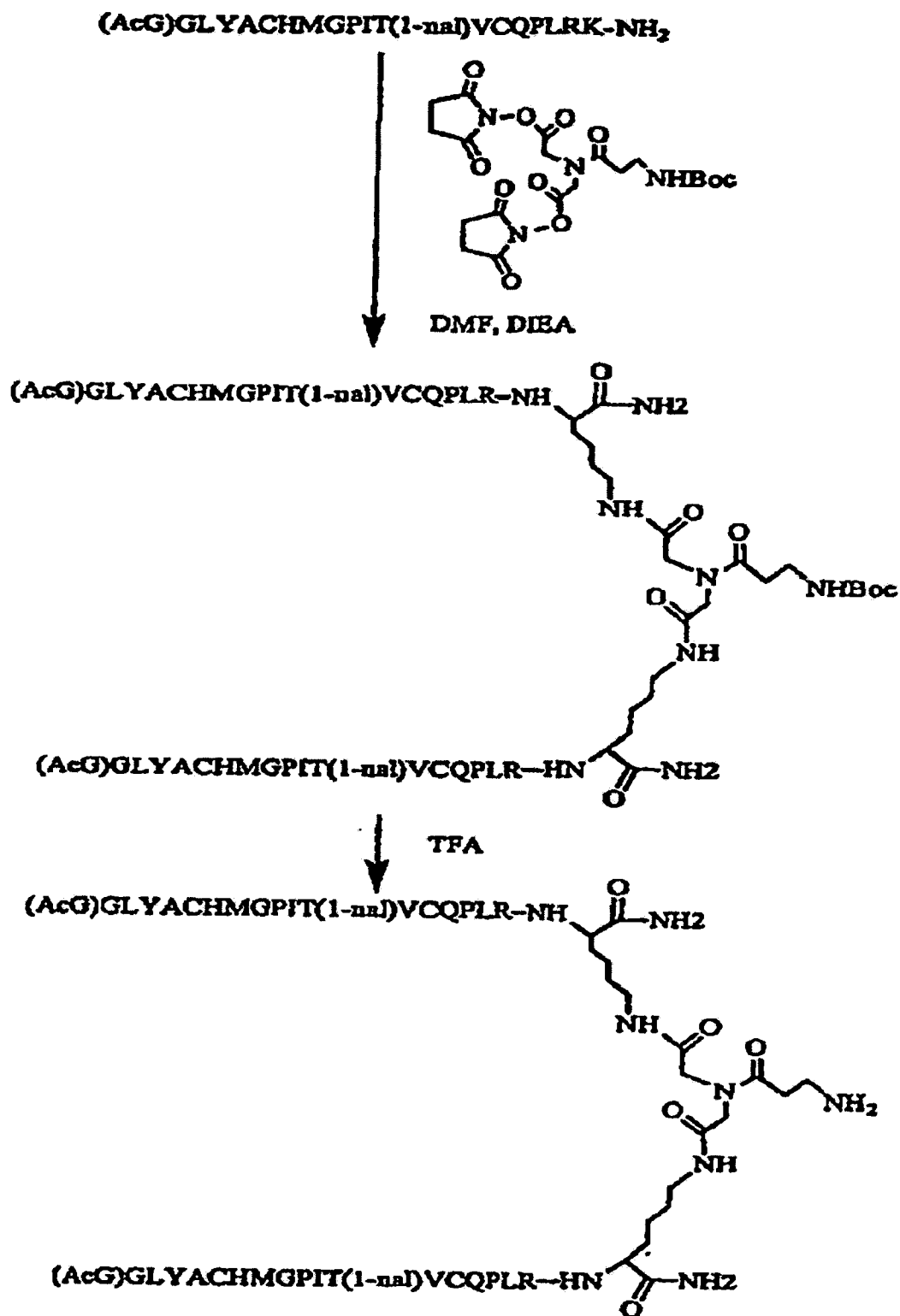


FIG. 16B

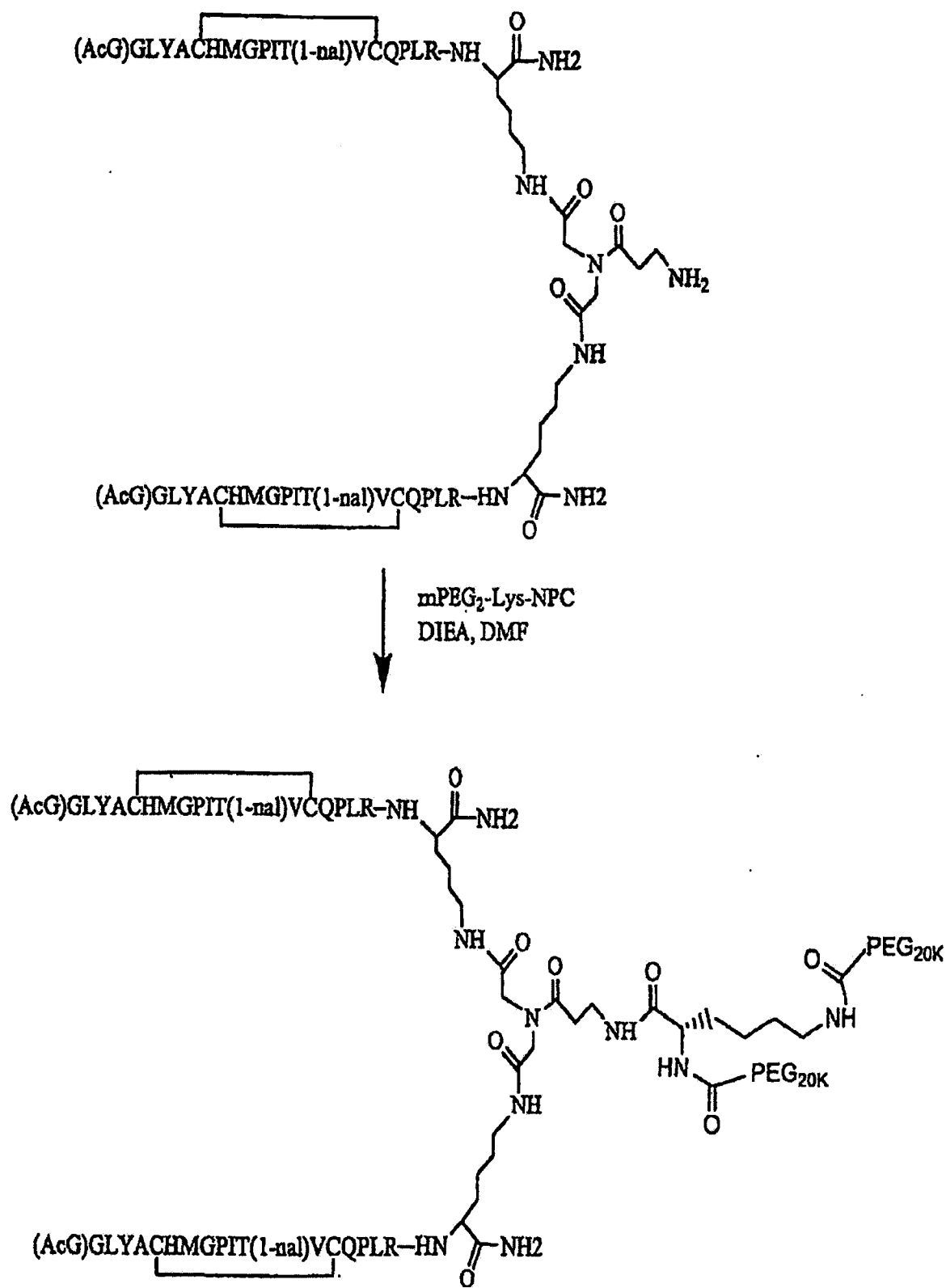


FIG. 16C

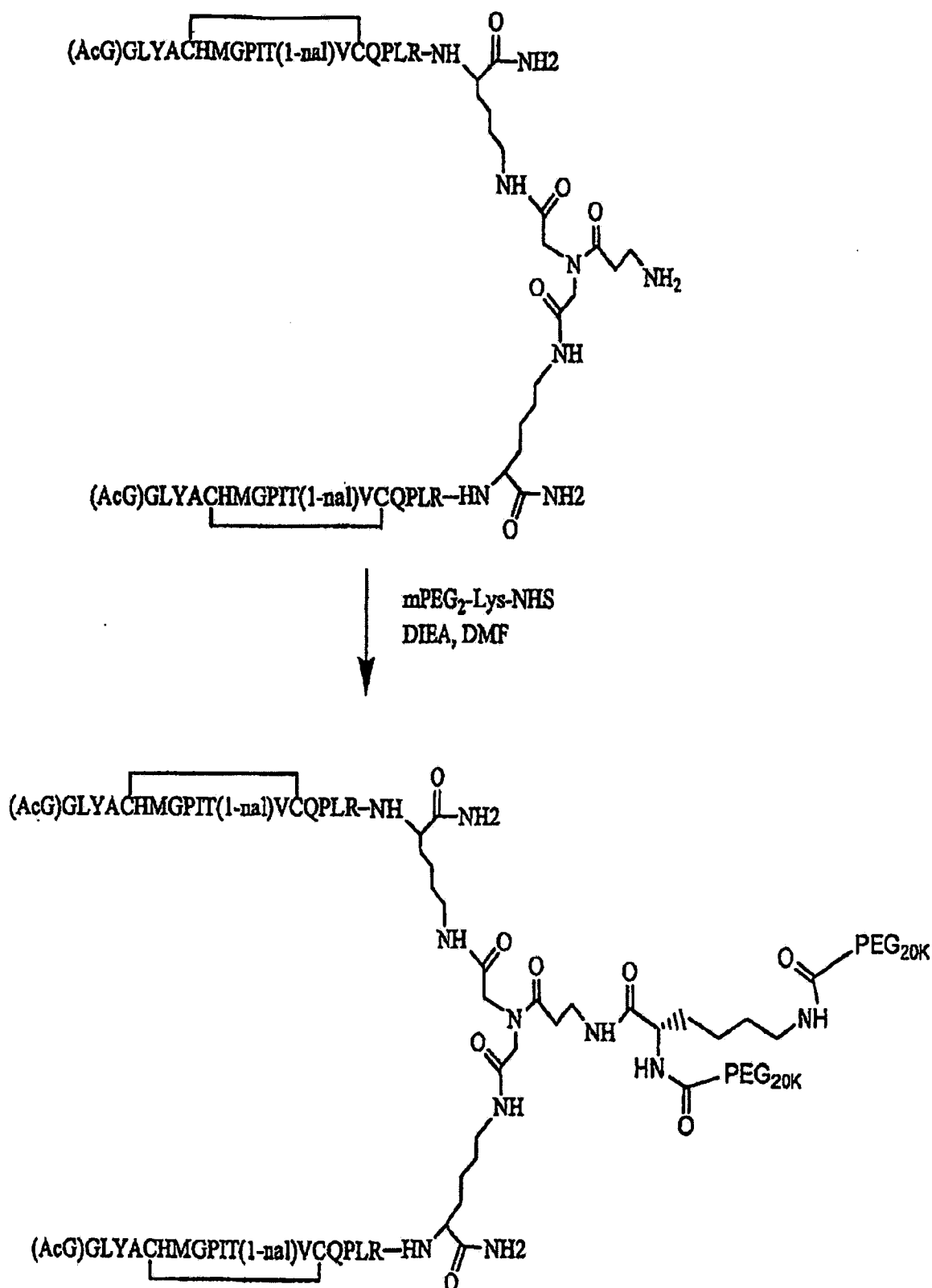


FIG. 16D